# Updates from ORD National Center for Environmental Assessment (NCEA) & Integrated Risk Information System (IRIS)

Tina Bahadori, NCEA Director
Kris Thayer, NCEA IRIS Division Director

EPA Science Advisory Board
August 29-30, 2017

# NCEA's Assessments at EPA

## NCEA's unique and essential role:

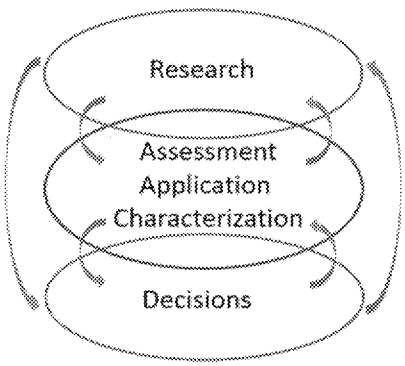
- Experienced and multi-disciplinary teams integrating and synthesizing findings from large bodies of evidence to develop scientific assessments
- Translating research and communicating scientific findings to inform Agency and State and local agency partner decisions

## Critically positioned between:

- Researchers – inside and outside EPA -- who are generating new findings and data

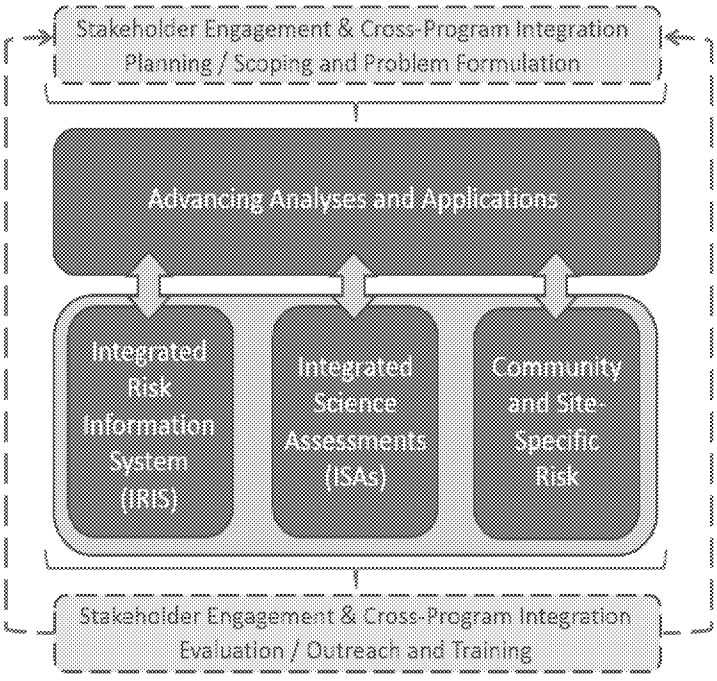
**AND**

- EPA Program and Regional offices, states and local agencies who must make regulatory, enforcement, and remedial actions and decisions



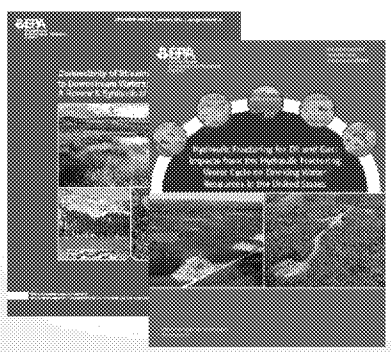

https://www.epa.gov/risk

# NCEA Human Health Risk Assessment



# NCEA Environmental Assessments

- **High profile assessments support regulatory and policy decisions for Office of Water, Regions and States**
  - Support to OW & Regions to develop benchmarks for conductivity
  - Assessment of Mountaintop Mining that provided support for OW guidance and action under CWA 404(c)
  - Evaluation of potential impacts of large-scale mining activities on salmon resources in Bristol Bay, Alaska

  - Connectivity of Waters of the United States: Synthesis of the scientific evidence on the connectivity of streams, wetlands, and open waters to downstream waters; scientific foundation for rulemaking to clarify CWA jurisdiction.
  - Hydraulic Fracturing Drinking Water Assessment

**NCEA continues to work with OW to translate science to effective policy, guidance, rules, and regulatory action.**

# New Leadership Structure in NCEA

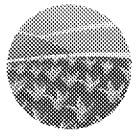
- **In January 2017, EPA appointed new leadership to the National Center for Environmental Assessment and to its IRIS Program.**
  - With significant experience in the chemical industry, and formerly the Director of ORD's Chemical Safety for Sustainability National Research Program, the new NCEA Director brings knowledge of TSCA, innovative applications of computational toxicology, and exposure science.
  - As a recognized leader in systematic review, automation, and chemical evaluations, the new IRIS Program Director brings experience in early partner and stakeholder engagement and input, and demonstrated actions to increase capacity and transparency in assessments.
- **Improved responsiveness and accountability through Senior Leadership Team**
  - NCEA IO
  - Divisions
  - Integrating across the spectrum of human and ecological RA practices

- Created in 1985 to foster consistency in the evaluation of chemical toxicity across the Agency.
- IRIS assessments contribute to decisions across EPA and other health agencies
- Toxicity values
  - Noncancer: Reference Doses (RfDs) and Reference Concentrations (RfCs).
  - Cancer: Oral Slope Factors (OSFs) and Inhalation Unit Risks (IURs).
- IRIS is the only federal program to provide toxicity values for both cancer and noncancer effects.
- IRIS assessments have no direct regulatory impact until they are combined with
  - Extent of exposure to people, cost of cleanup, available technology, etc.
  - Regulatory options, which are the purview of EPA's program offices.

# IRIS Addresses Agency Priorities and Mandates

IRIS

- Clean Air Act (CAA)
- Safe Drinking Water Act (SDWA)
- Food Quality Protection Act (FQPA)
- Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA)
- Resource Conservation and Recovery Act (RCRA)
- Toxic Substances Control Act (TSCA)

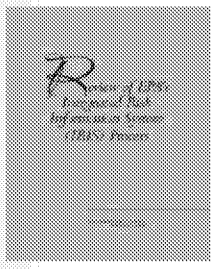


Broad Input to Support →

- Agency Strategic Goals
- Children's Health, Environmental Justice

# National Academy of Sciences (2014) Overarching Statements

2014



"Overall, the committee finds that substantial improvements in the IRIS process have been made, and it is clear that EPA has embraced and is acting on the recommendations in the NRC formaldehyde report. The NRC formaldehyde committee recognized that its suggested changes would take several years and an extensive effort by EPA staff to implement. Substantial progress, however, has been made in a short time, and the present committee's recommendations should be seen as building on the progress that EPA has already made." [p.9]

" . . . the IRIS program has moved forward steadily in planning for and implementing changes in each element of the assessment process. The committee is confident that there is an institutional commitment to completing the revisions of the process . . . Overall the committee expects that EPA will complete its planned revisions in a timely way and that the revisions will transform the IRIS Program." [p.135]

## Previous Phased Improvements to the IRIS Program

- The IRIS Program has taken prior, incremental steps to address the NAS recommendations, including:
- Revising the structure of assessments to enhance the clarity and transparency of presentation:
  - detailing the methods underlying each step of draft development (e.g., literature search strategy)
  - restructuring the document into separate hazard identification and dose-response chapters
  - replacing lengthy study summaries with synthesis text, supported by standardized tables and graphs
- Implementing "IRIS Enhancements", which laid out an updated process for developing and reviewing assessments that increases public input and peer consultation at earlier stages of assessment development, and clarifies processes for considering new evidence and scientific issues

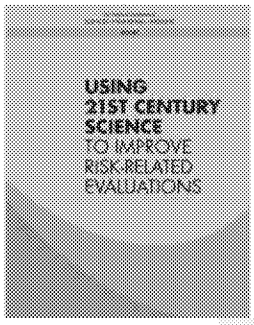
## Previous Phased Improvements to the IRIS Program

- Establishing the SAB Chemical Assessment Advisory Committee (CAAC) to strengthen peer review advice
  - 5 IRIS assessments completed CAAC review since 2014
- Contracting with the NAS to arrange for independent experts to attend public meetings on science topics
- Restructuring the IRIS program to create expertise-specific workgroups and improved assessment oversight

## How is IRIS Focusing?

- **Increase transparency and full implementation of systematic review**
  - implement using approaches that foster consistency across the IRIS program; many active and all new starts address ALL SR-related recommendations of 2014 NRC report
- **Modernize the IRIS Program**
  - through automation and machine learning to expedite systematic review, incorporation of emerging data types
- **Modularize product lines**
  - implement a portfolio of chemical evaluation products that optimize the application of the best available science and technology. These products will allow IRIS to remain flexible and responsive to clients within the EPA as well the diverse collection of stakeholders beyond EPA, including states, tribal nations, and other federal agencies.
- **Enhance accessibility**
  - provide outreach and training to make systematic review practices ubiquitous and more accessible; enhance data sharing through publicly available software platforms for assessments developed by EPA, other federal and state agencies, industry, academia and other third-parties.

# Other IRIS Improvements

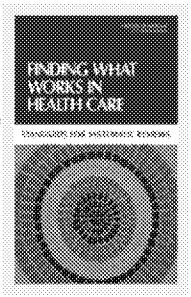



## Next Generation IRIS

- IRIS in the 21st Century – implement recommendations of the NAS 2017 report, Using 21st Century Science to Improve Risk-Related Evaluations;
- Collaborate with EPA's National Center for Computational Toxicology (NCCT) to build expert-judgement case studies that inform assessment development and fill gaps in assessments, especially for data poor chemicals; inform where resources should be strategically invested to generate additional data.

## Improved Management Practices

- Create efficiencies – engage other agencies to share common practices, data, and tools, and more efficiently leverage resources across the federal government.
- Improve timeliness and responsiveness – deploy program and project management tools to more effectively and efficiently utilize human resources to ensure timely delivery of products.



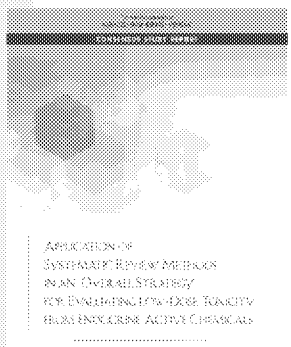

# A structured and documented process for transparent literature review[1,2]

*"… systematic review is a scientific investigation that focuses on a specific question and uses explicit, pre-specified scientific methods to identify, select, assess, and summarize the findings of similar but separate studies. The goal of systematic review methods is to ensure that the review is complete, unbiased, reproducible, and transparent"*

[1] Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act. EPA-HQ-OPPT-2016-0654. https://www.epa.gov/sites/production/files/2017-06/documents/prepubcopy_tsca_riskeval_final_rule_2017-06-22.pdf

[2] Institute of Medicine. Finding What works in Health Care: Standards for Systematic Reviews. p.13-34. The National Academies Press. Washington, D.C. 2011

# NAS (2017): Reflections and Lessons Learned from the Systematic Review




"….one disadvantage in conducting a systematic review is that it can be time and resource intensive, particularly for individuals that have not previously conducted a systematic review." [p.157]

"The committee discussed at length whether it could provide EPA with advice about when a systematic review should be performed but decided it could not be more specific because that decision will depend on the availability of data and resources, the anticipated actions, the time frame for decision making, and other factors." [p.157]

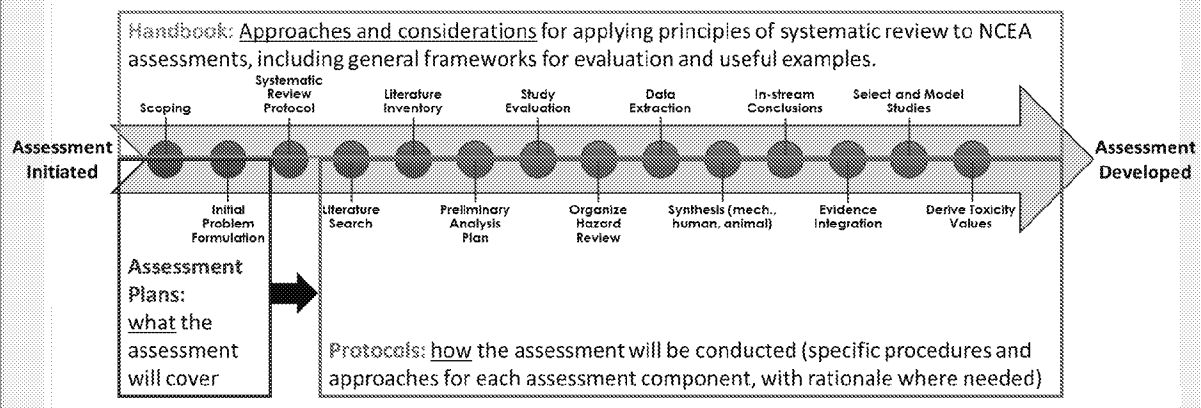
"The committee also recognized that it might be advantageous for EPA to build on existing systematic reviews that are published in the peer-reviewed literature." [p.157]

"The committee recognizes that the methods and role of systematic review and meta-analysis in toxicology are evolving rapidly and EPA will need to stay abreast of these developments, strive for transparency, and use appropriate methods to address its questions." [p.157]

## Making Systematic Review Pragmatic and Feasible For IRIS

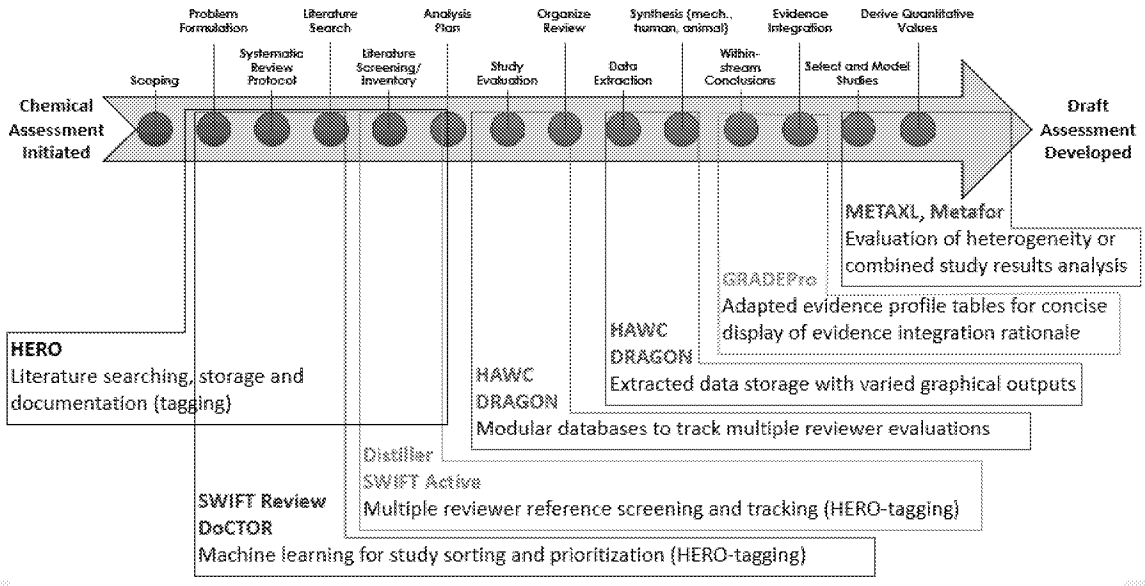
- Standard operating procedures (IRIS Handbook) and chemical-specific protocols
- Use of specialized software applications and automation
- Targeted focus, especially for evidence-rich topics
  - Make better use of well-conducted existing assessments as starting point
- Multiple assessment products ("modularity")
- Solicit early feedback during scoping and problem formulation via assessment plans
  - Summary of scoping and initial problem formulation conclusions, objectives and specific aims of the assessment, draft PECO (Population, Exposure, Comparators, and Outcomes) framework that outlines the evidence considered most pertinent to the assessment, and identification of key areas of scientific complexity
- Utilize iterative protocols to ensure focus on best-available and most-informative evidence as the assessment progresses

# Systematic Review Methods



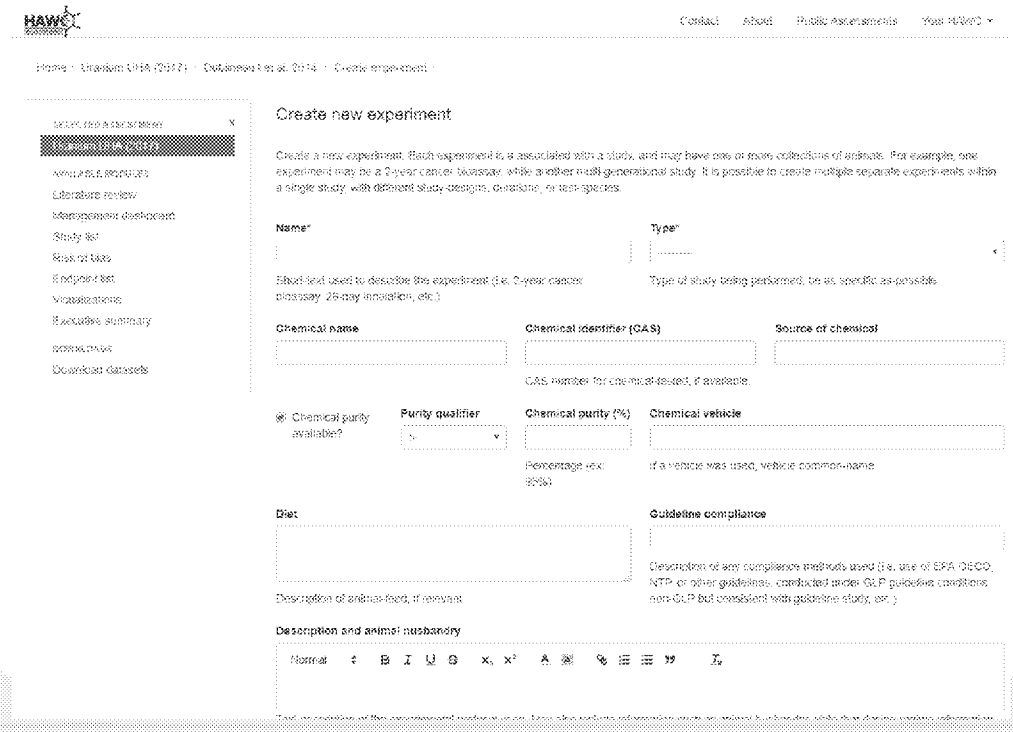

These documents should address previous discussions and suggestions made from during previous SAB reviews related to transparency of literature review and other aspects of the assessment (e.g., ammonia, trimethylbenzenes, ETBE/TBA)

# Systematic Review Tools

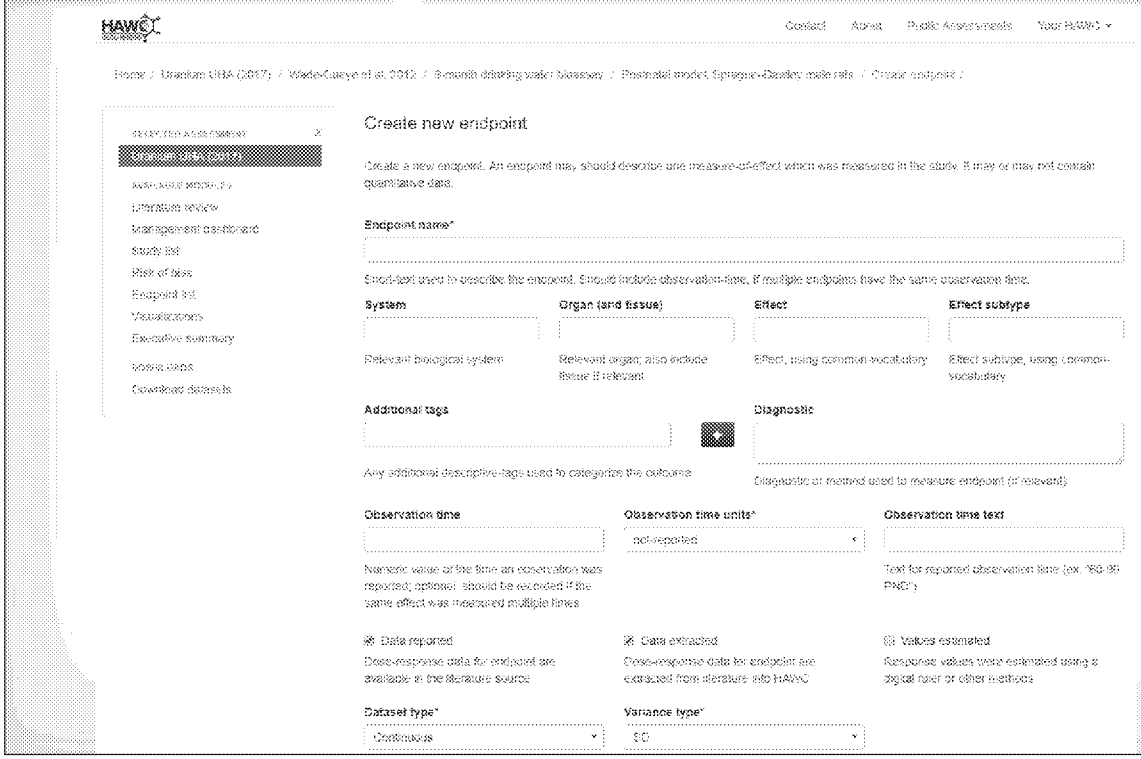



Tools repository: systematicreviewtools.com

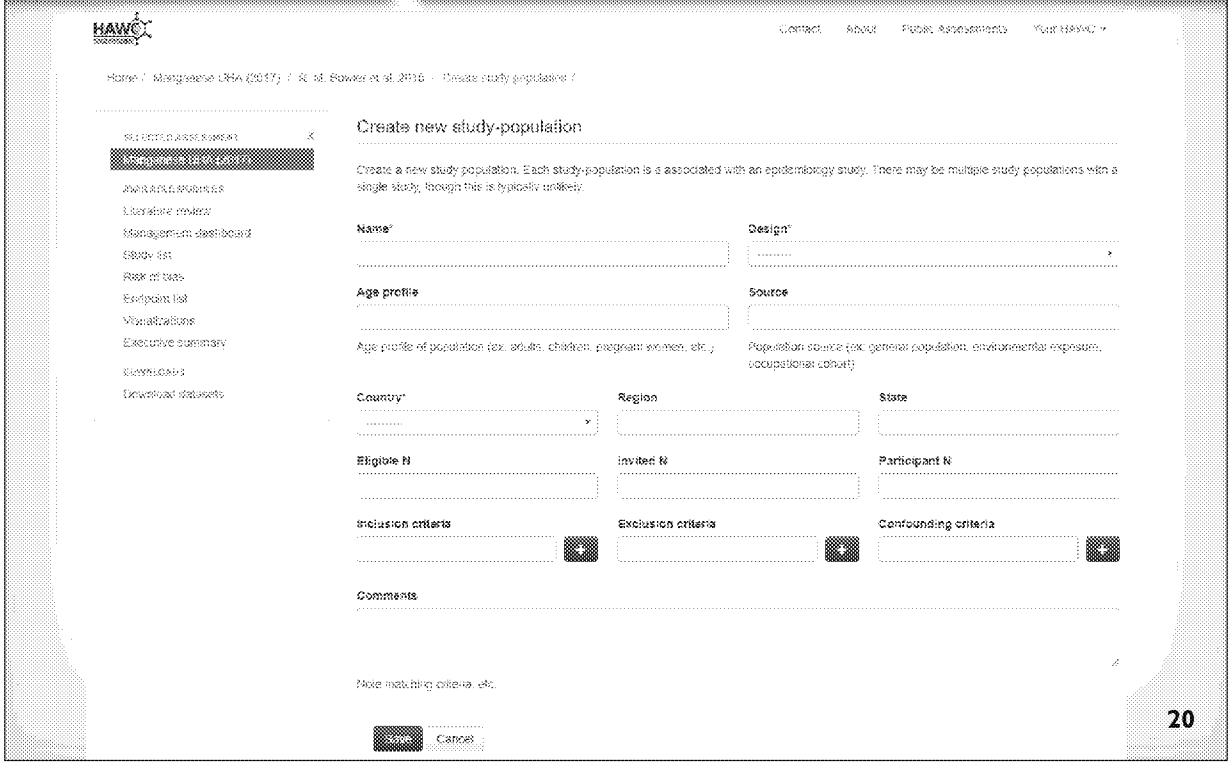
# HAWC: Data Extraction Animal Bioassay



# HAWC: Data Extraction Animal Bioassay



# HAWC: Data Extraction Epidemiology



# Epidemiology: Click to See More Display

"Identifying Research Needs for Assessing Safe Use of High Intakes of Folic Acid"

## Draft: Eczema, Prospective Studies

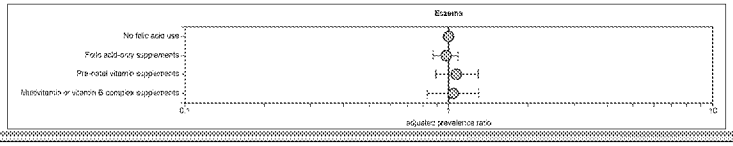
| Study | Population Name | Assessed Outcome Name | Exposure Measure | Exposure Comparison Statistical |
|---|---|---|---|---|
| Bekkers, 2012 | PIAMA birth cohort, 1996-1997 | Eczema | | |
| Dunstan, 2012 | Pregnant women in Western Australia | Eczema | | |
| Dunstan, 2012 | Pregnant women in Western Australia | Eczema | | |
| Dunstan, 2012 | Pregnant women in Western Australia | Eczema | | |
| Magdeljns, 2011 | KOALA Birth Cohort Study | Eczema until | | |
| Magdeljns, 2011 | KOALA Birth Cohort Study | Eczema until | | |
| Magdeljns, 2011 | KOALA Birth Cohort Study | Eczema until | | |

Bekkers, 2012 / PIAMA birth cohort, 1996-1997 / Folic acid containing supplements during pregnancy / Eczema

| | |
|---|---|
| Assessed outcome | Eczema |
| Population description | PIAMA birth cohort, 1996-1997 |
| Diagnostic | self-reported |
| Diagnostic description | an itchy rash that came and went on typical eczema sites (the folds of the elbows or behind the knees, around ears or eyes or in front of the ankles) |
| Risk finding supported? | inconclusive |
| Prevalence /incidence | 0.180 - 0.142, reported by age (Table 2) |
| Statistical metric presented | adjusted prevalence ratio |
| Statistical metric description | Longitudinally, generalised estimating equations (GEEs) with a log link function were used to obtain prevalence ratios (PRs). GEEs take into account the correlation between repeated measurements on the same individual. An im dependent correlation structure was used, due to the other outcome measures. An interaction term with age was included in the GEE model to allow the association between maternal use of supplements and the outcomes to vary with age. |
| Statistical power sufficient? | not reported or calculated |
| Dose response trend? | not applicable |
| Effect tags | dermal, hypersensitivity, immunological |
| Adjustment factors | • maternal allergy<br>• maternal education<br>• maternal smoking during pregnancy<br>• number older siblings |

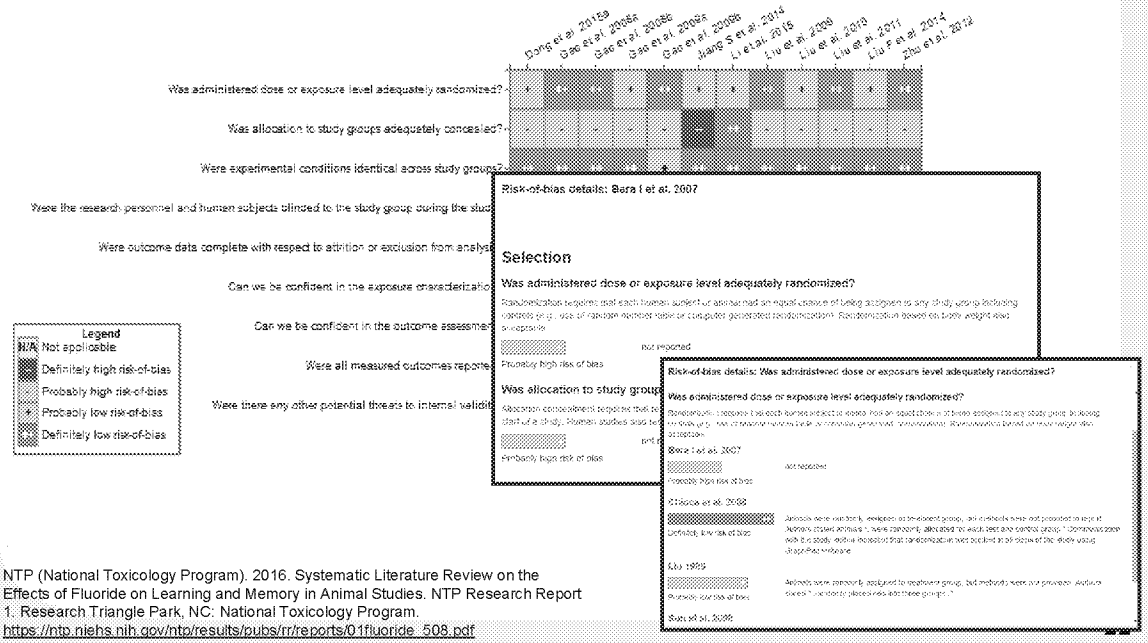
| Exposure group | N | Adjusted prevalence ratio | p-value |
|---|---|---|---|
| No folic acid use | 1902 | 1.0 | n.a. |
| Folic acid only supplements* | 1996 | 0.99 (0.87, 1.09) | n.s. |
| Pre-natal vitamin supplements | 297 | 1.07 (0.89, 1.29) | n.s. |
| Multivitamin or vitamin B complex supplements | 199 | 1.04 (0.83, 1.3) | n.s. |

* Main finding re-adjusted by RAWG assessment authors




NTP Monograph: Identifying Research Need
51. http://ntp.niehs.nih.gov/ntp/ohat/folicacid/

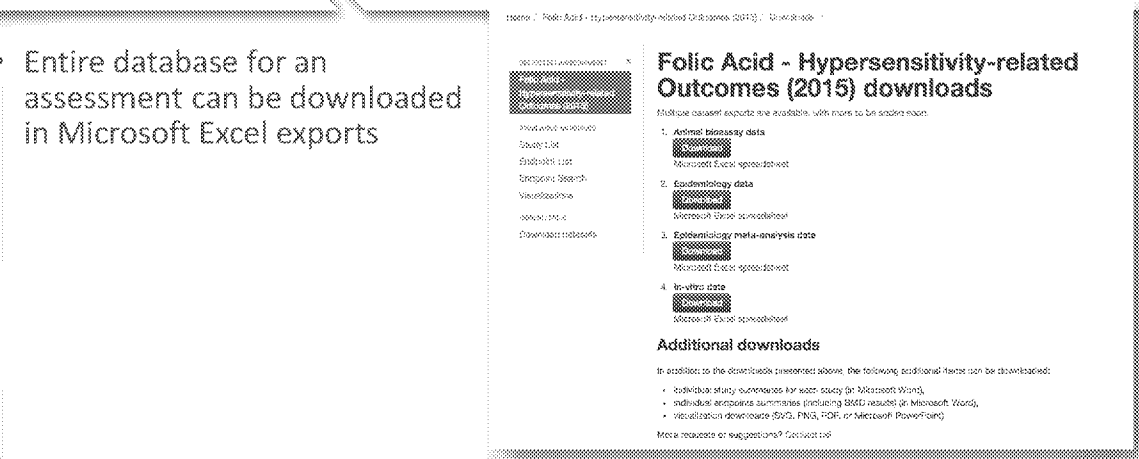
# HAWC: Risk of Bias

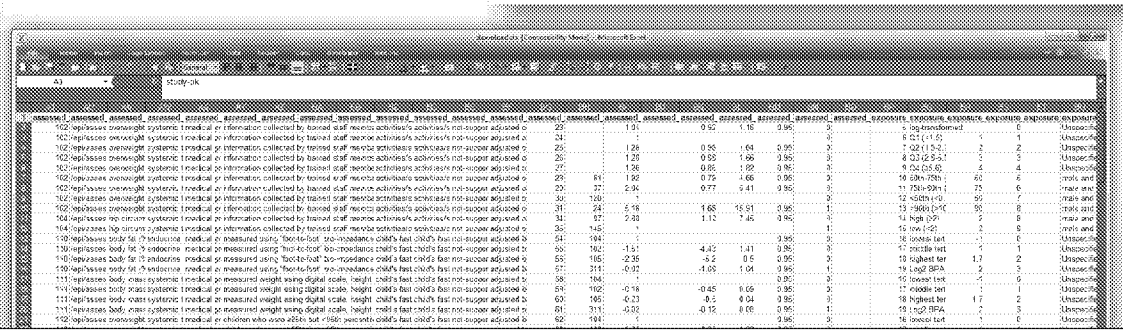


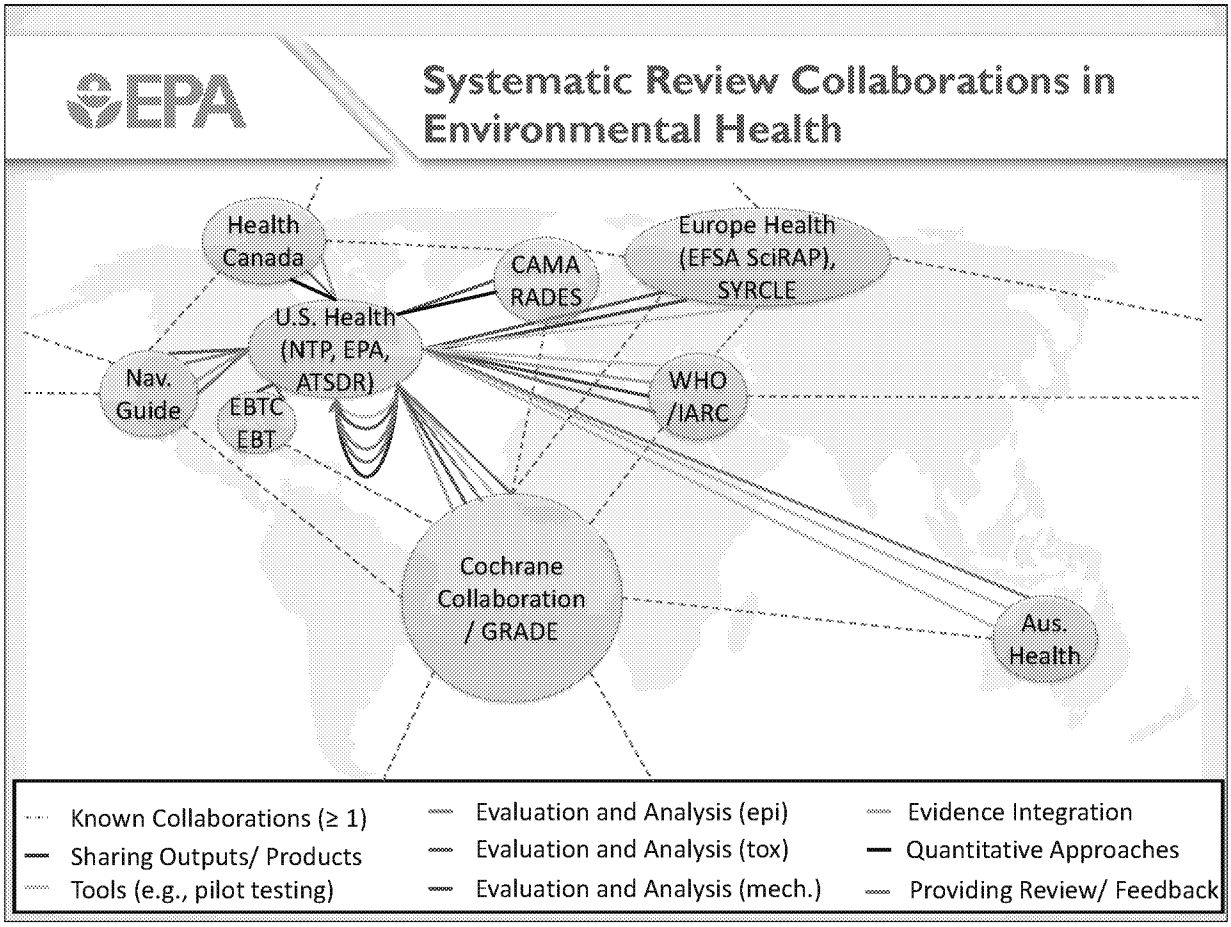

NTP (National Toxicology Program). 2016. Systematic Literature Review on the Effects of Fluoride on Learning and Memory in Animal Studies. NTP Research Report 1. Research Triangle Park, NC: National Toxicology Program. https://ntp.niehs.nih.gov/ntp/results/pubs/rr/reports/01fluoride_508.pdf

# HAWC: Download Reports

- Entire database for an assessment can be downloaded in Microsoft Excel exports




EPA
Systematic Review Collaborations in Environmental Health
Health Canada
CAMA RADES
Europe Health (EFSA SciRAP), SYRCLE
U.S. Health (NTP, EPA, ATSDR)
Nav. Guide
EBTC EBT
WHO /IARC
Cochrane Collaboration / GRADE
Aus. Health
Known Collaborations (≥ 1)
Sharing Outputs/ Products
Tools (e.g., pilot testing)
Evaluation and Analysis (epi)
Evaluation and Analysis (tox)
Evaluation and Analysis (mech.)
Evidence Integration
Quantitative Approaches
Providing Review/ Feedback

# IRIS Multi-Year Agenda

**Developing Agenda**

- **Released to the public December 2015**
- **Survey EPA program and regional offices for their assessment needs**
- **Estimate the resources needed for each assessment by science discipline**
- **Discuss with senior EPA officials how to meet the most high-priority needs**
- **Allocation of IRIS resources based on the plan**
- **Evaluate annually for continued relevance**

| Group | Chemicals |
|---|---|
| 1 | Manganese |
| | Mercury/methylmercury |
| | Nitrate/nitrite |
| | Perfluoroalkyl compounds |
| | Vanadium and compounds |
| 2 | Acetaldehyde |
| | Ammonia (oral) |
| | Cadmium and compounds |
| | Uranium |
| 3 | Di-(2-ethylhexyl) phthalate |
| | Dichlorobenzene isomers |
| | Methyl t-butyl ether (MTBE) |
| | Nickel and compounds |
| | Styrene |

| | |
|---|---|
| **Systematic review and implementation within the IRIS Program** | **Kris Thayer and Andrew Kraft** *National Center for Environmental Assessment* |
| **Discussion** | **Kenneth Ramos and CAAC Members** |
| **Public Comments** | **Registered Speakers** |

| | | |
|---|---|---|
| | **Assessment Plans and their Role within the IRIS Process** | **Jason Fritz** *National Center for Environmental Assessment* |
| Multi-year agenda group 1 → | **Nitrates/Nitrites** | **Larissa Pardo** *National Center for Environmental Assessment* |
| Discussed in public during 2014; (re-confirmed as current Agency need) → | **Ethylbenzene** | **Paul Reinhart** *National Center for Environmental Assessment* |
| Small evidence base (targeted update to address Agency need) → | **Chloroform** | **Ted Berner** *National Center for Environmental Assessment* |

***Draft assessment plans for 4 other multi-year agenda group 1 or 2 chemicals planned for 2018 public consultation**

# Open Discussion